Anal. Calculated for $C_{16}H_{25}NO_5$: C, 61.71; H, 8.09; N, 4.50. Found: C, 61.73; H, 8.30; N, 4.44.

As a further proof of structure the urethane moiety in III was hydrolyzed to the primary amine in the following way: A solution of III (150 mg.) in ethanol (3 ml.) and 2 *N* sodium hydroxide (2 ml.) was heated at reflux overnight, then diluted with water and extracted with chloroform. The combined extracts were dried (sodium sulfate) and evaporated. The residue, 67 mg. of oil, was dissolved in ether and saturated with hydrogen chloride gas. The precipitated salt was purified by recrystallization from ethanol to yield pure 2(2-ethyl-3,4,5-trimethoxyphenyl)ethylamine hydrochloride, m.p. 148–150°.

Anal. Calculated for $C_{13}H_{22}ClNO_3$: C, 56.62; H, 8.04; N, 4.94. Found: C, 56.60; H, 8.25; N, 5.15.

5-Ethyl-8-methoxycorydaldine (3,4-Dihydro-5-ethyl-6,7,8-trimethoxy-1-(2H)-isoquinolone) (IV).—A mixture of III (1.33 g.) and polyphosphoric acid (13 g.) was heated at 120° for 1.5 hr., then ice and water (50 ml.) was added and the mixture extracted with five 50-ml. portions of chloroform. The extracts were washed with saturated sodium chloride solution, combined, and dried over magnesium sulfate. After the solvent was evaporated, the residue, 230 mg. of yellow oil, was chromatographed on 15 g. of Woelm alumina (activity IV). Benzene, followed by chloroform eluted 154 mg. (14%) of crystalline IV, which after recrystallization from ethyl acetate melted at 127–129°.

An analytical sample was prepared by short-path distillation at 160° and 0.05 mm., $\nu_{max}^{CCl_4}$ 3300, 1680, and 1580 cm.$^{-1}$, λ_{max}^{EtOH} 217, 255, and 292 mμ (ϵ 43,000, 8,550, and 1,720 respectively).

Anal. Calculated for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.47; H, 7.27; N, 5.22.

5-Ethyl-8-hydroxycorydaldine (3,4-Dihydro-6,7-dimethoxy 5-ethyl-8-hydroxy-1-(2H)-isoquinolone (V).—Elution with chloroform–methanol (50:1) gave crystalline V (54 mg.), which, after recrystallization from ethyl acetate, melted at 177–179°. A sample sublimed at 0.05 mm. (170° bath) showed infrared bands at $\nu_{max}^{CCl_4}$ 3600, 3500, 1660, and 1580 cm.$^{-1}$ and ultraviolet absorption at λ_{max}^{EtOH} 220, 266 mμ (ϵ 37,500, 10,900 respectively) and gave a deep blue color with ferric chloride solution.

Anal. Calculated for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: 62.09; H, 6.84; N, 5.72.

3,4-Dihydro-5-ethyl-6,7,8-trihydroxy-1-(2H)-isoquinolone (VI).—5-Ethyl-8-methoxycorydaldine (IV) (375 mg.) was heated to reflux under nitrogen with 8 ml. of acetic acid and 2 ml. of 40% aqueous hydrogen bromide solution for 4 hr., and the solution evaporated to dryness *in vacuo*. The crystalline residue was triturated with ether and chloroform and recrystallized from 4 ml. of ethanol yielding 217 mg. (72%) VI, as colorless needles, m.p. 215–217°. An analytical sample was prepared by repeated recrystallization rom ethanol, m.p. 222–223°; ν_{max}^{KBr} 1640, 1615, 1600, 1510, cm.$^{-1}$, λ_{max}^{EtOH} 278 and 320 mμ (ϵ 9,900 and 3,100 respectively) dark blue color with alcoholic ferric chloride.

Anal. Calculated for $C_{11}H_{13}NO_4$: C, 59.18; H, 5.87; N, 6.28. Found: 59.16; H, 5.96; N, 6.20.

3,4-Dihydro-1-methyl-6,7,8-trimethoxyisoquinoline Hydrochloride (VIII).—N-Carbethoxy-2-(2-acetyl-3,4,5-trimethoxyphenyl)ethylamine (II) (1 g.) was heated to reflux with 6 *N* hydrochloric acid (3 ml.) and ethanol (3 ml.) for 6 hr. The ethanol was evaporated and the residue diluted with water (10 ml.) and extracted with six 10-ml. portions of chloroform. After drying (sodium sulfate) the solvent was evaporated and the residue leached with ether. The insoluble part, VIII (375 mg.), melted at 156–158° after recrystallization from a mixture of acetonitrile and ethyl acetate and showed infrared bands at $\nu_{max}^{CHCl_3}$ 1650, 1600, and 1570 cm.$^{-1}$. The ether-soluble part was mostly unchanged starting material (II).

1-Methyl-1,2,3,4-tetrahydro-6,7,8-trimethoxyisoquinoline Hydrochloride (IX).—A mixture of VIII (160 mg.) and platinum oxide (50 mg.) in 5 ml. of acetic acid was hydrogenated at room temperature and atmospheric pressure. After one molecular equivalent of hydrogen was consumed (1 hr.), the reaction stopped; the catalyst was filtered off, and the solvent evaporated. The residue was recrystallized from ethyl acetate and gave 80 mg. of IX as colorless crystals melting at 148–150°. $\nu_{max}^{CHCl_3}$ 1600 and 1500 cm.$^{-1}$.

N-Carbethoxy-1-methyl-1,2,3,4-tetrahydro-6,7,8-trimethoxyisoquinoline (VII).—To a solution of IX (80 mg.) in 2 ml. of water was added ethyl chloroformate (0.05 ml.) and a few drops of 2 *N* sodium hydroxide. The mixture was shaken in a test tube for 30 min. and then extracted with chloroform. After drying over magnesium sulfate the solvent was evaporated to yield 90 mg. of VII as a colorless oil. The purity of the sample was substantiated by a single spot on a thin-layer chromatogram. The R_f value and the infrared spectrum were identical with those of VII, the less polar hydrogenation product of N-carbethoxy-2-(2-acetyl-3,4,5-trimethoxyphenyl)ethylamine (II) (see below).

When the hydrogenation of II was conducted in such a way that the reaction was slow, VII was the major product as exemplified by the following example: 10% palladium-on-charcoal catalyst (100 mg.) in acetic acid (5 ml.) was saturated with hydrogen at room temperature and a solution of II (300 mg.) was then added in 5 ml. of acetic acid and the hydrogenation continued for 3 days. Only 1 equivalent of hydrogen was consumed. The catalyst was removed by filtration and the solution evaporated under reduced pressure. After partitioning the residue between chloroform and saturated sodium bicarbonate solution, the organic layer was dried (magnesium sulfate) and the solvent evaporated. The crude product was chromatographed on 6 g. of acid-washed alumina (Merck). Benzene–pentane (1:1) mixture eluted pure XII. (240 mg.) as a colorless oil.

An analytical sample was prepared by short-path distillation at 160° and 0.05 mm.; $\nu_{max}^{CCl_4}$ 1700, 1600 cm.$^{-1}$.

Anal. Calculated for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 61.86; H, 7.58; N, 4.46.

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Migration of Terminal Double Bond in the Course of Huang-Minlon Reduction

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A synthesis of the hitherto unknown 16-heptadecenoic acid (VII) was attempted, because this acid was regarded as a potential intermediate for the preparation of several lipide materials. The reaction sequence is illustrated in the flow sheet. However, the unexpected 15-heptadecenoic acid (V) was obtained as a result of double bond migration in the Huang-Minlon reduction.[1]

The 2-acylcyclohexanone (III) was prepared from 10-undecenoyl chloride (I) and *N*-(1-cyclohexenyl)morpholine (II) according to the pro-

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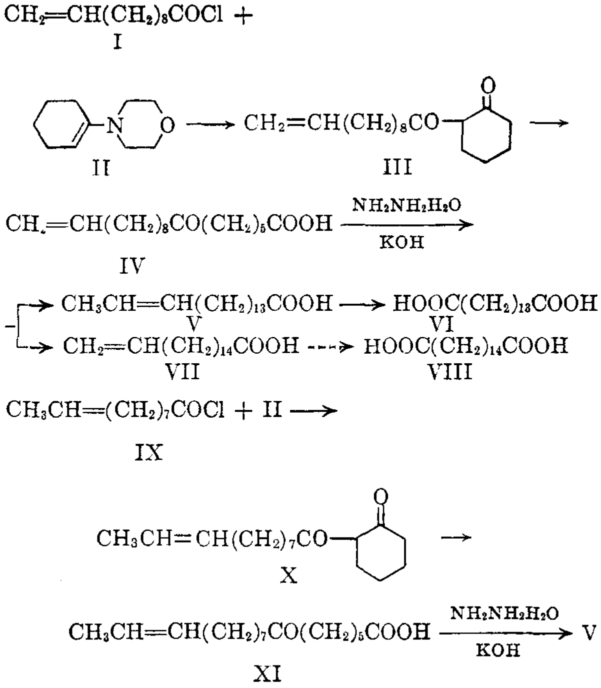
[1] Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).



cedure described by Hünig and co-workers[2] and III was cleaved with alkali to give 7-keto-16-heptadecenoic acid (IV). The Wolff–Kishner reduction according to the procedure as modified by Huang-Minlon[1] gave 15-heptadecenoic acid (V) in a fair yield. The proof of the constitution was furnished by the oxidative cleavage to afford tridecane-1,13-dicarboxylic acid (VI) melting at 113.5°.[3] The oxidation of 16-heptadecenoic acid (VII) would give tetradecane-1,14-dicarboxylic acid (VIII) melting at 124.1°.[4] The migration of the terminal double bond was shown to be due to the strongly basic condition of the medium in the Huang-Minlon procedure, since infrared spectrum of IV had absorption of a terminal vinyl group at 995 and 915 cm.$^{-1}$. 9-Undecenoyl chloride (IX) was similarly treated with II to give another keto acid (XI), which showed the marked depression of melting point when admixed with IV. The absorption at 995 and 915 cm.$^{-1}$ were absent in XI. However, XI gave the unsaturated acid V when it was reduced in the same manner as described for IV.

Attempted reduction of the keto acid IV by the Clemmensen–Martin–Sherman method[5] yielded a complicated product which was not further investigated. The Wolff–Kishner reduction of IV according to the method described by Kapp and Knoll[6] gave the same rearranged product in a slightly impure state.

It has been already established that 10-undecenoic acid rearranges to the 9-isomer by the treatment with alkali over 200°.[7] This rearrangement has now been shown to occur under the milder conditions of the Huang-Minlon procedure. Similar rearrangement of 9-decenoic acid into the 8-isomer in a nearly 90% yield has been reported previously.[8] It was also observed[8] that 2-allylcyclohexane-1,3-dione gave 7-nonenoic acid together with a small amount of the 8-isomer when the dione was treated according to the experimental procedure described by Stetter and Dierichs[9] including a modified Huang-Minlon reduction.

Among the hitherto published syntheses in which the Wolff–Kishner reduction of an ω-unsaturated keto acid gives an ω-unsaturated fatty acid,[6,10] the migration of the terminal double bond has never been recognized. It might be concluded that the reexamination of the structure would be necessary as to the position of the double bond in an unsaturated fatty acid derived from an ω-unsaturated keto acid so far as the Wolff–Kishner reduction, especially the Huang-Minlon modification, is included in the synthesis.

Amidst the possible isomers of *n*-heptadecenoic acids only three of them have been known, namely 2-,[11] 8-,[12] and 9-heptadecenoic acids.[13,14] 15-Heptadecenoic acid here synthesized may be enrolled as a newcomer of heptadecenoic acids. Although infrared spectrum showed a marked absorption band at 968 cm.$^{-1}$, this acid is regarded as an equilibrium mixture of *cis* and *trans* isomers in view of the condition of its formation.[7]

Experimental[15]

Rearrangement of 10-Undecenoic Acid into 9-Undecenoic Acid.—This rearrangement was carried out under basic conditions similar to the Huang-Minlon procedure but without hydrazine hydrate. A mixture of 36.8 g. of commercial undecenoic acid and 67.6 g. of potassium hydroxide dissolved in 320 ml. of diethylene glycol was similarly treated as described for 8-decenoic acid[8] and the resulting crude unsaturated acid was purified by esterification followed by saponification. Ethyl 9-undecenoate, b.p. 138–139° (17 mm.), n^{25}D 1.4395, giving correct analyses for carbon and hydrogen, has a marked absorption band at

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(2) S. Hünig, E. Lücke, and E. Benzing, *Ber.*, **91**, 129 (1958); S. Hünig and E. Lücke, *ibid.*, **92**, 652 (1959).

(3) P. Chuit and H. Hausser, *Helv. Chim. Acta*, **9**, 264 (1926).

(4) D. A. Fairweather, *Phil. Mag.* [7] **1**, 944 (1926).

(5) *Cf.* L. F. Fieser, *J. Am. Chem. Soc.*, **70**, 3197 (1948).

(6) R. Kapp and A. Knoll, *ibid.*, **65**, 2062 (1943).

(7) (a) I. V. Egorov, *J. Russ. Phys. Chem. Soc.*, **46**, 975 (1914); (b) A. Eckert, *Monatsh.*, **38**, 1 (1917); (c) A. Lüttringhaus and W. Reif, *Ann.*, **618**, 221 (1958); (d) R. G. Ackman, P. Linstead, B. J. Wakefield, and B. C. L. Weedon, *Tetrahedron*, **8**, 221 (1960).

(8) K. Sisido, M. Kawanisi, K. Kondô, T. Morimoto, A. Saitô, and N. Hukue, *J. Org. Chem.*, in press.

(9) H. Stetter and W. Dierichs, *Ber.*, **85**, 1061 (1952).

(10) (a) E. Stenhagen, *Arkiv Kemi*, **1**, No. 13, 99 (1949); (b) R. E. Bowman and W. D. Fordham, *J. Chem. Soc.*, 3945 (1952); (c) W. F. Huber, *J. Am. Chem. Soc.*, **73**, 2730 (1951).

(11) W. M. Lauer, W. J. Gensler, and E. Miller, *ibid.*, **63**, 1153 (1941).

(12) P. C. Mitter and P. N. Bagchi, *J. Indian Chem. Soc.*, **18**, 461 (1941).

(13) D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 1079 (1951).

(14) The presence of 6-isomer in the human hair lipide was suggested, but the more detailed information was not available [A. W. Weitkamp, A. M. Smiljanic, and S. Rothman, *J. Am. Chem. Soc.*, **69**, 1936 (1947)].

(15) All temperatures are uncorrected. Microanalyses were performed by Miss Kenko Ogawa.

968 cm.$^{-1}$ but not at 990 and 910 cm.$^{-1}$. Ames and Bowman[16] reported b.p. 87–89° (0.5 mm.), n^{20}D 1.4406 for ethyl *trans*-9-undecenoate. Saponification of the ester furnished 9-undecenoic acid, b.p. 139° (6.5 mm.), n^{26}D 1.4500, in an 88.9% yield based on the starting acid. Iodine value (Wijs): 138.0; calculated for undecenoic acid: 138.4. Infrared spectrum (liquid film) had a distinct absorption at 968 cm.$^{-1}$, not at 990 and 910 cm.$^{-1}$ [reported[16] for *trans*-9-undecenoic acid, b.p. 121–123° (0.7 mm.), n^{20}D 1.4519]. *p*-Phenylphenacyl ester prepared in the usual manner[17] melted at 62.5–63.5° after a single recrystallization from ethanol and gave correct analyses for carbon and hydrogen. Ames and Bowman[16] reported m.p. 64.5–65° for the *p*-phenylphenacyl ester of *cis*-9-undecenoic acid.

7-Keto-16-heptadecenoic Acid.—To a solution of 18.4 g. (0.11 mole) of N-(1-cyclohexenyl)morpholine[18] and 10.9 g. (0.12 mole) of triethylamine in 140 ml. of chloroform was added 20.3 g. (0.1 mole) of 10-undecenoyl chloride[6] in 50 ml. of chloroform over a period of 1 hr. at 35°, and the mixture was maintained at this temperature for an additional 3 hr. The acylated enamine was hydrolyzed in the chloroform solution by refluxing with 50 ml. of 20% hydrochloric acid for 5 hr. and the chloroform layer was separated and washed with water until pH of washing water became 6. The aqueous layer combined with the washings was neutralized to pH 6 with concentrated sodium hydroxide solution and extracted twice with 50-ml. portions of chloroform. The combined chloroform solutions were evaporated to dryness under diminished pressure and the residue was decomposed with 20 g. of potassium hydroxide in 15 ml. of water on a boiling water bath for 10 min. Semisolid material thus obtained was dissolved in 1 l. of hot water and strongly acidified with concentrated hydrochloric acid. The precipitates were collected by filtration, washed with 100 ml. of cold water, and dried. Recrystallizations from *n*-hexane gave the keto acid, m.p. 68.5–69.3°, weighing 27.0 g. (92.7%). ν_{max} (Nujol) at 1710 (broad), 995 and 915 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found: C, 72.35; H, 10.74.

Semicarbazone prepared by the usual method[19] melted at 110–111.2° after a single recrystallization from ethanol.

Anal. Calcd. for $C_{18}H_{33}O_3N_3$: C, 63.68; H, 9.80. Found: C, 63.65; H, 9.99.

15-Heptadecenoic Acid.—A solution of 14 g. (0.05 mole) of the aforementioned keto acid, 20 ml. of 80% hydrazine hydrate, and 2.8 g. of potassium hydroxide dissolved in 50 ml. of diethylene glycol was heated under reflux for 8 hr. The hot solution was added with 14 g. of potassium hydroxide and 50 ml. of diethylene glycol, and water as well as excess hydrazine hydrate were removed by distillation. The temperature of the content rose gradually up to 185°, when the mixture was heated under reflux for an additional 15 hr. The reaction mass was dissolved in 1.5 l. of water and strongly acidified with concentrated hydrochloric acid. The resulting precipitates were collected after cooling, washed with ice-cold water and dried. Recrystallizations from acetone and *n*-hexane afforded 12.9 g. (86.2%) of colorless leaflets melting at 49.5–50.3°. ν_{max} (Nujol) at 968 cm.$^{-1}$.

Anal. Calcd. for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 75.89; H, 12.00.

p-Phenylphenacyl ester[17] melted at 86.0–87.0° after two recrystallizations from ethanol.

Anal. Calcd. for $C_{31}H_{42}O_3$: C, 80.47; H, 9.15. Found: C, 80.28; H, 9.01.

Oxidation of 15-Heptadecenoic Acid.—To a solution of 2 g. of the unsaturated acid in 20 ml. of glacial acetic acid was added portionwise 6 g. of chromic acid under vigorous stirring and the mixture was heated under reflux for an additional 1 hr. The reaction mixture was added with 20 ml. of ethanol and evaporated *in vacuo*. The residue was treated with 100 ml. of dilute hydrochloric acid, then with 5% aqueous sodium hydroxide solution, and filtered. When the filtrate was acidified with hydrochloric acid, there separated a white precipitate, which was collected, washed with water, and dried. On recrystallizations from ethyl acetate and glacial acetic acid there was obtained 0.5 g. of tridecane-1,13-dicarboxylic acid, m.p. 112.5–113.5° (reported[3] m.p. 113.5°), which gave correct analyses for carbon and hydrogen.

7-Keto-15-heptadecenoic Acid.—A mixture of 9-undecenoyl chloride[6] and 13.5 g. of N-(1-cyclohexenyl)morpholine was similarly treated as described for 10-undecenoyl chloride, and 17.2 g. of 7-keto-15-heptadecenoic acid, m.p. 70.0–71.5°, was obtained as colorless crystals in a 90% yield after recrystallizations from *n*-hexane. ν_{max} (Nujol) at 970 cm.$^{-1}$. Mixed m.p. with 7-keto-16-heptadecenoic acid was 61.5–64.5°.

Anal. Calcd. for $C_{17}H_{30}O_3$: C, 72.30; H, 10.71. Found: C, 72.17; H, 10.76.

Semicarbazone prepared similarly melted at 111.5–112.8° after recrystallizations from ethanol and showed a marked depression of m.p. when admixed with the semicarbazone of 7-keto-16-heptadecenoic acid.

Anal. Calcd. for $C_{18}H_{33}O_3N_3$: C, 63.68; H, 9.80. Found: C, 63.85; H, 10.01.

The keto acid was reduced in the same manner as described for 7-keto-16-heptadecenoic acid and the unsaturated acid, m.p. 49.5–50.3°, was obtained in an 85.6% yield. Mixed m.p. with the specimen obtained as above showed no depression. The *p*-phenylphenacyl ester of both origin, when admixed, also did not show any depression of melting point.

Reduction of 7-Keto-16-heptadecenoic Acid by the Usual Wolff–Kishner Method.—A mixture of 5.6 g. of the keto acid, 2.8 g. of metallic sodium, and 2.9 g. of hydrazine hydrochloride in 80 ml. of anhydrous ethanol was heated at 185–200° for 96 hr. in a closed vessel as described by Kapp and Knoll[6] and 3.0 g. of unsaturated acid, m.p. 49.0–50.1°, was isolated after several recrystallizations from acetone, petroleum ether (b.p. 40–60°), and aqueous methanol. Mixed m.p. with aforementioned 15-heptadecenoic acid showed no depression. *p*-Phenylphenacyl ester of this unsaturated acid melted at 85.9–87.0° and gave correct analyses for carbon and hydrogen. Mixed m.p. with the ester derived from 15-heptadecenoic acid showed no depression.

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[16] D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 677 (1952).

[17] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley & Sons, Inc., New York, 1956, p. 200.

[18] S. Hünig, E. Benzing, and E. Lücke, *Ber.*, **90**, 2833 (1957); G. Optiz, H. Hellman, and H. W. Schubert, *Ann.*, **623**, 112 (1959).

[19] Ref. 17, p. 218.

A Seven-Membered Cyclic Ketal of Pyridoxol[1]

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Cyclic ketals are important intermediates in the chemistry of polyhydroxy compounds, notably carbohydrates, and their formation and stability are of considerable theoretical and practical interest. Acetonation of pyridoxol can conceivably

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[1] Pyridoxine Chemistry III; for preceding papers in this series, see ref. 3 and W. Korytnyk and E. J. Kris, *Chem. Ind.* (London), 1834 (1961).